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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,256	09/13/2005	Angus Moodycliffe	112843-066	3290

29157 7590 12/06/2006

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/525,256	MOODYCLIFFE ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *4,5 and 9-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-27-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Sequence Rule Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

CFR §1.821(d) reads as follows:

> Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims or the patent application.

Pages 18-19 and 30 of the instant specification contain nucleic acid sequences which are not preceded by "SEQ ID NO:". Applicants are reminded that the nucleic acid sequences shown in the specification must be entered in the paper copy of sequence listing as well as CRF. See Notice to Comply. Any response to this action must correct this deficiency, as this requirement will not be held in abeyance.

Response to Arguments/Election

Applicant's election with traverse of claims 1-3 and 6-8 drawn to a substance capable of blocking endogenous CD_{1d} function wherein the substance is a polynucleotide antisense to glycosylceramide synthase mRNA in the reply filed on November 13, 2006 is acknowledged.

The traversal is on the ground(s) that the restriction requirement separating 32 claims into 22 alleged groups of inventions is improper. This is not found persuasive for the reasons stated below:

1) The number of claims does not govern the number of inventive groups in a patent application. The groupings of claims do depend on the number of distinct/independent inventions claimed in a patent application. That is, a patent application containing a single claim can be properly restricted to a number of inventive groups, if the single claim is found to contain multitudes of distinct and independent inventions as is the case with the instant application. See below for further explanation.

2) The alleged Markush-type claim to five different types of substances recited in claims 1 and 6 is improper because the five substances do not share any common core structure nor do they target the same gene/protein. For instance, a lipid has no structural or functional similarity to an antisense polynucleotide, and by the same token, phosphatidylinositol phosphate is a distinct gene/protein from glucosylceramide synthase. Hence, there is no single structural similarity among the claimed substances, and therefore the claimed substances do not belong to the same art-recognized class of compounds. MPEP §2173.05(h) clearly states, "The materials set forth in the Markush group ordinarily must belong to a recognized physical or chemical class or to an art-recognized class". Accordingly, the instantly claimed subgenera of substances are independent and distinct and thus the alleged "Markush claim" is improper. Hence, claim 1, in and of itself, contains five distinct inventions. See pages 5-6 of the Office action mailed to the applicant on October 13, 2006, for example.

3) The instant application is filed under 35 U.S.C. 371 and 37 CFR 1.495, which therefore is subject to the "unity of invention" rule. For applicant's own edification, see MPEP

Chapter 1800 regarding 37 CFR §1.475, for example. Because the instant application was restricted under the unity of invention rule, the issue of "unduly burden" was neither stated nor asserted in the Office action mailed to the applicant on October 13, 2006. Further, as indicated in the Office action of October 13, 2006, it is determined that there is neither unity of invention nor a special technical feature that contributes over the teachings of the prior art. See page 5. Since the instant application is not a U.S. filed application, the rules stated in MPEP §803 regarding search burden/workload does not apply, thus applicant's argument is irrelevant and moot.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Claims 4-5, 9-32, a polynucleotide antisense to CD_{1d} mRNA, a polynucleotide sense to the ceramide synthase mRNA, a polypeptide or peptide, and a lipid are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Accordingly, claims 1-32 are pending, and claims 1-3 and 6-8 pertaining to a polynucleotide antisense to the glucosylceramide synthase mRNA are currently under examination on the merits.

Specification

The disclosure is objected to because of the following informalities:

1) It contains sequence rule non-compliant subject matter on pages 18-19 and 30. See Notice to Comply.

2) The figure shown on page 36 of the specification must be entered in "Drawings". Page 36, line 7 clearly states "see figure below", thus the disclosure represented in lines 10-20 of page 36 should be assigned a proper Figure No.

3) Pages 30, 35, and 37-38 contain tabulated disclosure, which should have been appropriately assigned Table Numbers. See for example pages 23-24, which contain appropriately assigned Tables Nos.

Appropriate correction is required.

Claim Objections

Claims 1 and 6 are objected to for containing non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and /or chemical properties, functional characteristics, structure/function correlation, or any combination thereof.

In the instant case, the breadth of claims 1-3 and 6-8 embraces any and all genera of polynucleotide antisense substances/compositions comprising any target sequence of the glucosylceramide synthase gene/mRNA. Since there is more than one species of the glucosylceramide synthase gene (see the HomoloGene citation), the specification must reasonably convey to one skilled in the art that the inventors were in possession of any polynucleotide antisense targeted to any species of genes homologous to the claimed glucosylceramide synthase gene.

As such, the specification must provide a representative number of the broadly claimed genera of the polynucleotide antisense substances in order to provide evidence of possession of the claimed genera. Although the specification provides primer sequences for GAPDH and CD_{1d} used for RT-PCR, the primer sequences bear no relevance to the claimed polynucleotide antisense. In fact, the instant specification is completely silent about the structures of the polynucleotide antisense substances targeted to the glucosylceramide synthase sequence. Moreover, regardless of the type of compositions as claimed in claim 7, the specification discloses no compositions comprising a polynucleotide antisense substance and milk, for instance, as claimed in claim 8. In fact, the entire disclosure of the specification, except for Example 13, is devoted to establishing a relationship between UV irradiation and CD_{1d}.

With regard to the claimed subject matter, "polynucleotide antisense targeted to the glucosylceramide synthase gene", the specification merely states that the number of the

glucosylceramide synthase transcripts may be reduced by designing a polypeptide antisense to at least a part of the glucosylceramide synthase gene or mRNA. See page 10. Further, this is the one and only occurrence where the term "glucosylceramide synthase" appears throughout the entire specification.

The claims also specifically claim a polynucleotide antisense targeted to the glucosylceramide synthase mRNA that is capable of blocking or modifying endogenous CD_{1d} function. The instant specification contains no exemplified species of such polynucleotide antisense that either block or upregulates or downregulates the endogenous CD_{1d} function. Since the word "modifying" embraces both "increasing" and "decreasing", the specification must provide sufficient distinguishing identifying characteristics of such claimed polynucleotide antisense that either increases or decreases the endogenous CD_{1d} function. Again, the specification discloses no physical structure of any polynucleotide antisense, let alone the structure/function correlation between the structure of polynucleotide antisense substances and the function of blocking or increasing or decreasing the function of endogenous CD_{1d}.

In light of the above, it is inarguably clear that the instant specification does not contain any disclosure of complete or partial structure of the broadly claimed polynucleotide antisense substance/composition, nor does it provide any structure/function correlation of the claimed substance/composition. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making it. The compound itself is required. See *Fiers v. Revel*, 984 F.2d 1164, 1168, 25 USPQ2d 1601,1604-05 (Fed. Cir. 1993). Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics of the claimed polynucleotide antisense/composition, the specification does not provide adequate written description of the claimed genus. In view of the foregoing, one of ordinary skill in the art

cannot ascertain that the inventors were in possession of any and all species of the claimed polynucleotide antisense/composition targeted to the glucosylceramide synthase gene/mRNA, at the time the instant application was filed.

See also *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991), which clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see page 1116).

Corollary to the instant claims to broad genus of polynucleotide antisense in the claims, in *Fiddes,* claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class since the specification provided only the bovine sequence (See *Fiddes v. Baird,* 30 USPQ2nd 1481 at 1483).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Line 2 of claim 2 recites, "reducing at least one of the transcription and translation of the CD_{1d} gene". It is vague and ambiguous what is meant by the phrase "at least one of the

transcription and translation", because such limitation requires that there must be more than one "transcription" and more than one "translation" of the CD_{1d} gene. Both transcription and translation are molecular processes, not products, and therefore, "transcription" and "translation" are not countable. It is unclear whether the applicants meant to claim "transcripts" by "transcription".

Claim 3 claims the substance according to claim 1 which is derived from a source chosen from the group consisting of plants, microbes, animals, ingredients of green tea and carotenoid. Claim 1 claims that the substance is the polynucleotide antisense because the antisense is the only element comprising the claimed substance. Hence, claim 3 claims a polynucleotide antisense to glucosylceramide synthase gene that is derived from plants, microbes, animals, ingredients of green tea and carotenoid. Given the broadest reasonable interpretation of the claim language, it is unclear how an antisense molecule can be derived from "ingredients" of green tea. Further, the glucosylceramide synthase gene is not known in the art to be present in plants. See the HomoloGene citation. Moreover, one skilled in the art cannot recognize the metes and bounds set forth by the term "ingredients" because there are multiple, different ingredients in green tea.

Claim 6 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Since claim 6 claims a composition containing a substance capable of blocking or

modifying endogenous CD_{1d} function without reciting any further ingredients or elements, the subject matter claimed in claim 6 is regarded identical to that claimed in claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, and 6 are rejected under 35 U.S.C. 102(a) as being anticipated by Di Sano et al. (*Cell Death and Differentiation,* June 2002, 9:693-695), as evidenced by Nieda et al. (*Human Immunology,* 1999, 60:10-19) and Balreira et al. (*British Journal of Haematology,* 2005, 129:667-676).

The claims are drawn to a substance/composition capable of modulating endogenous CD1d function, wherein the substance is a polynucleotide antisense to the glucosylceramide synthase gene (claims 1 and 6) that is derived from animals (claim 3).

Di Sano et al. teach a glucosylceramide synthase (GCS) antisense vector, which downregulates the glucosylceramide synthase activity as well as its mRNA expression when transfected into mammalian cells *in vitro* (page 693 and Figure 1).

Nieda et al. teach that specific glycolipids such as α-GalCer and α-GlcCer are recognized by Vα24TCRs on Vα24 NKT cells in a CD1d-restricted manner. They also teach the possibility that naturally occurring α-glycosylceramides, or molecules with similar structures in humans, are

ligands or can act as antigens presented by CD1d (entire document, for particulars, see Abstract and page 17). Accordingly, the inter-dependent relationship between CD1d and glycosylceramides was recognized in the art before the instant application was filed.

The reference of Balreira et al. is not a prior art; however, it is cited herein to establish the nexus between glucosylceramide synthase and CD1d in light of *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981): "To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill".

Balreira et al. teach that the inhibition of glucosylceramide activity in subjects *in vivo* by administering conduritol-B-epoxide results in increased levels of surface expression of CD1d, suggesting that glucosylceramide deficiency may preferentially influence the expression of CD1d at the cell surface monocytes (entire document, specially pages 672-674). Accordingly, the teachings of Balreira et al. substantiate the findings of Nieda et al. and further provide evidence that the expression of glucosylceramide regulates the expression of CD1d. In view of the foregoing, one of skill would recognize that it is an inherent property of glucosylcermide synthase to modulate CD1d function because CD1d expression is shown to be modulated by the glucosylceramide signaling pathway, which involves glucosylceramide synthase.

Since the GCS antisense vector of Di Sano et al. meets the structural limitations of the claimed substance, and since both Nieda et al. and Balreira et al. clearly establish the existence of the inter-dependent relationship between glycosylceramides and CD1d, it is concluded that the antisense vector of Di Sano et al. will inherently have the function of modulating endogenous CD_{1d} function, absent evidence to the contrary.

See *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), in which the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." *Id.*

See also *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Claims 1, 3, and 6 are rejected under 35 U.S.C. 102(a) as being anticipated by Deng et al. (*Glycobiology,* March 2002, 12:145-152), as evidenced by Nieda et al. (*Human Immunology,* 1999; 60:10-19) and Balreira et al. (*British Journal of Haematology,* 2005, 129:667-676).

The claims are described above.

The teachings of Nieda et al. and Balreira et al. are described above.

Deng et al. teach a vector containing a GCS antisense fragment that is obtained from human medulloblastoma cell RNA (page 146), which reduces the level of glucosylceramide expression in cells when transfected (page 147). Since the GCS antisense vector of Deng et al. satisfy the structural requirements of the claimed substance, and since both Nieda et al. and Balreira et al. clearly establish the existence of the inter-dependent relationship between

glycosylceramides and CD1d, it is concluded that the antisense vector of Deng et al. will inherently have the function of modulating endogenous CD_{1d} function, absent evidence to the contrary. See also *In re Crish* (Fed. Cir. 2004) and *Atlas Powder Co. v. Ireco Inc.* (Fed. Cir. 1999).

Claims 1, 3, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al. (*The Journal of Biological Chemistry,* March 2000, 275:7138-7143) and Balreira et al. (*British Journal of Haematology,* 2005, 129:667-676).

The claims are described above.

The teachings of Nieda et al. and Balreira et al. are described above.

Liu et al. teach a GCS antisense vector that decreases the level of GCS mRNA and protein when transfected into mammalian cells (entire document). Since the GCS antisense vector of Liu et al. satisfy the structural requirements set forth by the claims, and since both Nieda et al. and Balrerira et al. clearly establish the existence of the inter-dependent relationship between glycosylceramides and CD1d, the antisense vector of Liu et al. will inherently have the function of modulating endogenous CD_{1d} function, absent evidence to the contrary. See also *In re Crish* (Fed. Cir. 2004) and *Atlas Powder Co. v. Ireco Inc.* (Fed. Cir. 1999).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

TC1600
JANE ZARA, PH.D.
PRIMARY EXAMINER

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 37 CFR §1.821(g). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. §§1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. §§1.821-1.825. Applicants attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a Sequence Listing as required by 37 C.F.R. §1.821(c).
- [X] 3. A copy of the Sequence Listing in computer readable form has not been submitted as required by 37 C.F.R. §1.821(e).
- [ ] 4. A copy of the Sequence Listing in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. §1.822 and/or 1.823, as indicated on the attached copy of the marked-up Raw Sequence Listing.
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. §1.825(d).
- [ ] 6. The paper copy of the Sequence Listing is not the same as the computer readable from of the Sequence Listing as required by 37 C.F.R. §1.821(e).
- [ ] 7. Other:

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the Sequence Listing. (If the unidentified sequences are not provided on the CRF)
- [X] An initial or substitute paper copy of the Sequence Listing, as well as an amendment directing its entry into the specification. (If the unidentified sequences are not provided in the paper copy)
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). (If a new paper and/or CRF are required)

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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